



# UNITED STATES PATENT AND TRADEMARK OFFICE

MV

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,401	07/31/2001	Shoshana Merchav	01/22310	1613

7590 02/18/2004

G E Ehrlich  
Suite 207  
2001 Jefferson Davis Highway  
Arlington, VA 22202

EXAMINER

NAFF, DAVID M

ART UNIT	PAPER NUMBER
----------	--------------

1651

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	Application No. 09/890,401	Applicant(s) MERCHAV ET AL.	
	Examiner David M. Naff	Art Unit 1651	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 23 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☒ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attachment.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☒ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: None.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-20 and 51-70.

Claim(s) withdrawn from consideration: 21-50 & 71-99.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_



David M. Naff  
Primary Examiner  
Art Unit: 1651

Art Unit: 1651

ATTACHMENT TO FORM PTOL-303

The amendment raises new issues for consideration under 35 U.S.C. 112, second paragraph. Bridging lines 1 and 2 of step (a) of claim 1 and line 2 of step (i) of claim 51 "medium flow conditions" is uncertain as to meaning and scope. Does this mean that the flow conditions are "medium", or is this referring to a "medium" flowing through the bioreactor? If the former intended, this raises the issue of new matter since clear support is not found in the specification for flow conditions that are medium. If the latter is intended, it is unclear as to relationship of the medium to cell culture, and the conditions that are used for medium flow.

Step (b) of claim 1 and step (ii) of claim 51 are unclear as to when the cells are seeded in the bioreactor. Are the cells seeded before, during or after culturing of stromal cells?

The arguments and 37 CFR Declaration are unpersuasive. The declaration is unpersuasive since it fails to describe bioreactor structure and culture conditions in sufficient detail to enable determining whether the 3 fold increase is significant and whether the claims are commensurate in scope with the procedure used in the declaration according to the invention. The declaration does not describe the specific bioreactor structure used, and specific culturing conditions such as rate

Art Unit: 1651

of culture medium flow in the bioreactor and composition of the medium when culturing both stromal and stem cells. Also, it is unclear as to whether continuous flow is maintained during culturing both the stromal cells and stem cells or only during  
5 culturing the stromal cells. The declaration additionally fails to describe in detail the procedure used when culturing under static conditions that is being compared with.

Furthermore, Sussman et al and Stephanopoulos et al suggest that using non-woven fiber sheets and continuous flow culturing  
10 will result in better cell growth. As is apparent from Sussman et al, the fiber sheet provides increased attachment surface and provides adequate porosity for entrance of cells and nutrients and for removal of wastes (col 4, lines 46-66). These conditions would have been expected to result in better cell  
15 growth. Stephanopoulos et al disclose (col 3, lines 57-67) advantages of convective culture medium flow that would have been expected to result in better cell growth over when using static conditions. Continuous flow is obviously going to provide more nutrients to the cells and result in more cell  
20 growth than when using static conditions.

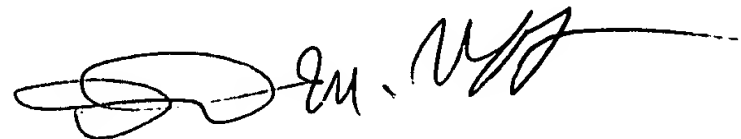
Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M.

Art Unit: 1651

Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff  
Primary Examiner  
Art Unit 1651

DMN  
2/13/04